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CERTIFICATE OF MAILING BY FIRST CLASS MAIL (37 CFR 1.8) Applicant(s): L.S. Mansfield, M.G. Rossano, A.J. Murphy and R.A. Vrable			Docket No. MSU 4.1-528	
Application No. 09/669,833	Filing Date 09/26/2000	Examiner Padmavathi Baskar	Customer No. 21036	Group Art Unit 1645

Invention: VACCINE TO CONTROL EQUINE PROTOZOAL MYELOENCEPHALITIS IN HORSES

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 09/669,833 Confirmation No. 2531

Applicants : Linda S. Mansfield, Mary G. Rossano, Alice J. Murphy, and Ruth A. Vrable

Filed : September 26, 2000

Title: VACCINE TO CONTROL EQUINE PROTOZOAL MYELOENCEPHALITIS IN HORSES

TC/A.U. : 1645

Examiner : Padmavathi Baskar, Ph.D.

Docket No. : MSU 4.1-528

Customer No. : 21036

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SUPPLEMENTAL BRIEF UNDER 37 C.F.R. § 41.37

Sir:

This is in response to the Notice of Non-Complaint Appeal Brief dated August 24, 2006. This is an appeal from a final rejection in the above entitled application. The claims on appeal are set forth as Claims Appendix. An oral hearing will be requested. The fee due upon filing of the Brief has been paid.

(1) Real Party in Interest

The real party in interest is the Board of Trustees operating Michigan State University, East Lansing, Michigan, a constitutional corporation of the State of Michigan, which is the assignee of the above entitled application.

(2) Related Appeals and Interferences

(a) The present application is a divisional application of:

Application Serial No. 09/513,086, filed February 24, 2000 (which claims benefit of a provisional patent Application No. 60/152,193, filed September 2, 1999). The '086 application relates to a vaccine comprising the 16 and 30 kDa antigens. Application Serial No. 09/513,086 is on appeal.

(b) The present application is also related to:

Application Serial No. 09/670,244 ('224) which relates to recombinant protein comprising the 16 ±4 and 30 ±4 kDa antigens;

Application Serial No. 09/670,355 ('355), relating to a vaccine comprising DNA encoding the 16 ±4 and 30 ±4 kDa

antigens;

Application Serial No. 09/669,843, relating to a monoclonal antibody which selectively binds to a *Sarcocystis neurona* antigen; and

Application Serial No. 09/670,096, relating to compositions and method for treating an equid infected with *Sarcocystis neurona* with antibodies against the 16 ±4 and 30 ±4 kDa antigens.

The '244 application has been abandoned. The '355 application was abandoned after an affirmation by the Board (enclosed). A decision by the Board is also enclosed for Application Serial No. 09/669,843, and for Application Serial No. 09/670,096. There are no other related appeals and interferences.

(3) Status of Claims

Claims 1-28 and 36-50 were cancelled in a preliminary amendment. Claims 31-35 were cancelled during prosecution of the application. Claims 29 and 30 were rejected in the final Office Action. Claim 30 was cancelled in an Amendment under 37 C.F.R. 1.116. Claim 29 remains pending in the application and is on appeal.

(4) Status of Amendments

An Amendment under 37 C.F.R. 1.116 was mailed on February 24, 2005. In the Amendment Claim 30 was cancelled. Claim 29 was amended to correct formal errors in sections (d) and (e). The amendment was entered by the Examiner in the Advisory Action mailed July 07, 2005. In the Advisory Action the rejection under 35 U.S.C. §112, second paragraph rejection was withdrawn.

(5) Summary of Claimed Subject Matter

The claimed subject matter in Claim 29 is a method for producing an antibody for use as a passive immunity vaccine in horses against a *Sarcocystis neurona* antigen selected from the group consisting of a 16 (+/-4) kDa antigen and a 30 (+/-4) kDa antigen, as determined by SDS polyacrylamide gel electrophoresis comprising:

(Support for this is found at page 5, lines 13-24; page 7, lines 21-30; page 10, lines 30-34; page 12, lines 31-35; page 15, lines 18-21; page 26, lines 20-26 of the specification.)

(a) providing a *Sarcocystis neurona* antigen selected from the group consisting of the 16 (+/-4) kDa antigen and the 30 (+/-4) kDa antigen;

(Support for this is found at page 5, lines 13-24; page 7, lines 21-30; page 10, lines 30-34; page 12, lines 31-35; page 15, lines 18-21; page 26, lines 20-26; Example 1 at page 33, lines 25-34 of the specification; Example 3 illustrates a method for the isolation, excystation and culture of *Sarcocystis neurona*; page 19, line 2 through page 23, line 6 of the specification teach a variety of examples of methods which can be used to prepare the antigens.)

(b) admixing the antigen with an adjuvant to produce an admixture;

(Support for this is found at page 26, lines 27 through page 27, line 3; page 34, lines 7-10 of the specification.)

(c) immunizing a mammal with the admixture to produce antibodies against antigen;

(Support for this is found at page 34, lines 7-10 of the specification.)

(d) removing serum from the immunized mammal and isolating from the serum the antibody against the *Sarcocystis neurona* antigen selected from the group consisting of the 16 kDa +/-4 antigen and the 30 kDa +/-4 antigen; and

(Support for this is found at page 34, lines 12-14 of the specification)

(e) providing the isolated antibodies to the 16 and 30 kDa antigen together as the passive immunity vaccine in horses.

(Support for this is found at page 5, lines 13-24.)

(6) Grounds of Rejection to Be Reviewed on Appeal

(a) Claim 29 was rejected under 35 U.S.C. §103(a) as being unpatentable over Liang *et al.* 1998 (*Infection and Immunity;* 66(5) 1834-1838) and Marsh *et al.* 1996 (*JAVMA,* 209: 1907-1913) in view of Prescott *et al.* (*AJVR* 1997, 58: 356-359) and Higuchi *et al.* 1999 (*Journal of Veterinary Medicine* 46, 641-648).

(b) Claim 29 was rejected under 35 U.S.C. §112, second paragraph as being vague and indefinite.

(7) Argument

A. The Examiner rejected Claims 29 under 35 U.S.C. §103(a) as being unpatentable over Liang *et al.* 1998 (*Infection and Immunity;* 66(5) 1834-1838) and Marsh *et al.* 1996 (*JAVMA,* 209: 1907-1913) in view of Prescott *et al.* (*AJVR* 1997, 58: 356-359) and Higuchi *et al.* 1999 (*Journal of Veterinary Medicine* 46, 641-648).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The cited prior art references do not teach or suggest all of the limitations of the claimed method. The cited references would not teach or suggest to a person of ordinary skill in the art a method for producing a passive immunity vaccine in horses with isolated antibodies to the 16 (+/-4) kDa antigen and the 30

(+/-4) kDa antigen of *Sarcocystis neurona* together. In addition, a prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Therefore, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). Liang *et al.* teaches away from a passive immunity vaccine with isolated antibodies to the 16 (+/-4) kDa antigen and the 30 (+/-4) kDa antigen of *Sarcocystis neurona* together.

Liang *et al.* teaches that serum and cerebrospinal fluid (CSF) from horses with a clinical diagnosis of a neurologic disorder resembling equine protozoal myeloencephalitis (EPM) reacted with combinations of Sn30, Sn16, Sn14, and Sn11 proteins from *Sarcocystis neurona* (*S neurona*) to form various band patterns on an immunoblot. The serum and CSF samples were grouped together by Liang *et al.* based upon the resulting band patterns. Liang *et al.* then teaches that *in vitro* neutralization assays against

Sarcocystis neurona merozoites isolated from bovine turbinate cell culture revealed "significant differences in inhibitory activities between the groups of serum and CSF samples with different immunoblot band patterns" (Liang *et al.*: page 1837, first full paragraph.) However, when Liang *et al.* correlated band patterns with inhibitory activities it was concluded that "no inhibitory activity correlating with antibody to Sn30 was noted." (Liang *et al.*: page 1836, first paragraph.) This can be clearly seen with sample N6 which recognizes the Sn30 protein of *Sarcocystis neurona*. (Liang *et al.*: Figure 2 on page 1836.) The teaching of Liang *et al.* therefore, would not show or suggest to a person of ordinary skill in the art that a passive immunity vaccine in horses with isolated antibodies to the 16 (+/-4) kDa antigen and the 30 (+/-4) kDa antigen of *Sarcocystis neurona* together should be pursued. A person of ordinary skill in the art would not be motivated to pursue the claimed method for producing the passive immunity vaccine after reading Liang *et al.* Liang *et al.* would actually lead a person of ordinary skill in the art away from the claimed invention, since *in vitro* neutralization assays against *Sarcocystis neurona* merozoites show that the Sn30 antigen

provides no inhibitory activity.

Marsh *et al.* 1996 does not add anything to the teachings of Liang *et al.* which would lead a person of ordinary skill in the art to the claimed invention. Marsh *et al.*, like Liang *et al.*, teach that serum and CSF samples from *Sarcocystis neurona* infected horses react with a protein band from *Sarcocystis neurona* merozoites of approximately 29 kDa. Marsh *et al.* further teaches that serum and CSF from a *Neospora* infected horse also apparently reacted with the 29 kDa protein band from *Sarcocystis neurona* merozoites. According to Marsh *et al.*, "the serologic evidence from the commercial laboratory's western blot test and results from the author's laboratory would indicate that the horse was coinfected with *Neospora* and *S neurona* or that antibodies produced from the *Neospora* infection cross-reacted to *S neurona* parasite antigens" (Marsh *et al.*: page 1911, right column, first full paragraph). Marsh *et al.* teaches that horses infected with *Neospora* can have antibodies which cross-react with this antigen so as to "have a false-positive reaction on the western blot assay for *S. neurona*, but that *Neospora*-infected horses can be specifically identified when they

also are tested for reactivity to *Neospora* antigens" (Marsh *et al.*: page 1911, right column at end of first full paragraph). This teaching by Marsh *et al.* would lead a person of ordinary skill in the art away from using the 30 kDa antigen from *Sarcocystis neurona* merozoites in a diagnostic test. Marsh *et al.* does not suggest to a person of ordinary skill in the art that a specific antibody to the 30 kDa antigen of *Sarcocystis neurona* is needed. The teachings of Marsh *et al.* only suggest that antibodies in the serum and CSF of *Neospora*-infected horses can cross-react with the 30 kDa antigen of *Sarcocystis neurona* in diagnostic tests. A person of ordinary skill in the art would in no way be motivated by Marsh *et al.* to produce an antibody to the 30 kDa antigen of *Sarcocystis neurona* for use as a passive immunity vaccine in horses by this teaching, alone or in combination with any of the other cited references.

Marsh *et al.* teaches "that *Neospora* sp should be considered in the differential diagnosis of EPM" (Marsh *et al.*: page 1912, left column, fourth full paragraph). This teaching of Marsh *et al.* would not motivate one of ordinary skill in the art to produce an antibody against the 30 kDa

antigen of *S. neurona* even for diagnostic purposes. According to Marsh *et al.* "pathologists need to be aware of morphologic differences in infections caused by *S. neurona* and *Neospora* sp. to avoid misdiagnosis." Marsh *et al.* conclude that there is a need for "confirmation of etiologic agents by use of immunohistochemical analysis, even when western blot results are positive for *S. neurona* antibodies (Marsh *et al.*: page 1912, right column, first paragraph). Marsh *et al.* base this conclusion on their own study, where they found tissue cysts in a *Neospora* infected horse which were "typical of *Sarcocystis* sp." (Marsh *et al.*: page 1912, left column, second full paragraph). Upon immunohistochemical staining of the tissue cysts, however, the cysts had a strongly positive reaction with polyclonal antiserum developed against the bovine *Neospora* sp tachyzoites, but the cysts did not react with the *S. neurona* antiserum. (Marsh *et al.*: page 1908, right column, first full paragraph; and Figure 2). Nothing about this approach for the confirmation of the etiologic agents by use of immunohistochemical analysis would lead a person of ordinary skill in the art to the claimed method for producing an antibody against the 16 kDa and 30 kDa antigens of

Sarcocystis neurona. Clearly, the *Neospora* sp antiserum and the *S. neurona* polyclonal antiserum were both used successfully to confirm the etiologic agent. Nothing would lead a person of ordinary skill in the art to isolate antibodies against specific 16 kDa and 30 kDa antigens of *Sarcocystis neurona* from the *S. neurona* polyclonal serum for even diagnostic purposes.

Prescott *et al.* teach passive immunization of foals against *Rhodococcus equi* pneumonia using plasma from a horse vaccinated with an acetone-precipitated, Triton X-extracted (APTX) antigen extracted from *R equi* with a high proportion of virulence-associated protein (VapA). Prescott *et al.* provide plasma for passive immunization, but Prescott *et al.* do not provide an antibody which has been isolated from the plasma as in the passive immunity vaccine of the claimed method. Prescott *et al.* teach that passive immunization with plasma from a vaccinated horse "appeared to enhance clearance of *R. equi* from the lungs of foals." (Prescott *et al.*: "Conclusions" on page 356, left column). However, Prescott *et al.* arrived at this conclusion "with considerable reservation because the number of foals used was low and 1 foal administered adult plasma without APTX

antibodies, but with a low residual titer of 10, cleared infection as well as did foals administered hyperimmune plasma." (Prescott *et al.*: page 358, first paragraph in right column). When the lung clearance in this foal was included with that in the other two foals given APTX antibody-negative plasma "there was no significant difference between this group and the group of foals given immune plasma." (Prescott *et al.*: "Passive immunization of foals against experimentally induced infection," page 357, right column). Therefore, a person of ordinary skill in the art would not likely pursue a passive immunity vaccine against *S. neurona* in horses after reading Prescott *et al.*

A person of ordinary skill in the art, after further reading of Prescott *et al.*, would question whether bacterial clearance data necessarily correlates with protection against *R. equi* pneumonia. Prescott *et al.* teach that *R. equi* is a cause of chronic pyogranulomatous pneumonia and lung abscesses in foals. (Prescott *et al.*: First paragraph on page 356, left column). Prescott *et al.* monitored lung clearance of bacteria to assess the effect of vaccination, because "despite heavy challenge exposure, pneumonic changes were not induced in any foal." (Prescott

et al.: "Discussion," page 358, right column). Prescott *et al.* further teaches that when foals are vaccinated with the APTX antigen in "contrast to the nonvaccinated foals, 4 of 8 vaccinated foals developed culture-confirmed *R. equi* pneumonia at 5 to 7 weeks of age." (Prescott *et al.*: page 358, first paragraph). Prescott *et al.* concludes that "paradoxically, vaccination of mares and their foals with APTX antigen did not protect foals and may have enhanced *R. equi* pneumonia in the foals." (Prescott *et al.*: "Conclusions" on page 356, left column). "At the time of development of pneumonia, these foals had a median serum ELISA titer of 2,560." (Prescott *et al.*: page 358, first paragraph). Since the IgG-ELISA containing the APTX antigen will detect IgG antibodies against the APTX antigen in the serum samples, a person of ordinary skill in the art would likely question whether boosting antibodies against specific antigens in horses would be useful for protecting against conditions such as *R. equi* pneumonia. (Prescott *et al.*: page 357, first paragraph). A person of ordinary skill in the art would therefore not be motivated to pursue a passive immunity vaccine in horses after reading Prescott *et al.*

Higuchi *et al.* teach passive immunization of foals

against *Rhodococcus equi* infection using hyperimmune plasma, but Higuchi *et al.* do not provide antibody which has been isolated from the plasma as in the passive immunity vaccine of the claimed method. While Higuchi *et al.* noted differences between foals receiving hyperimmune plasma and foals not receiving any plasma which suggest protection, "the differences observed were not statistically significant between the two groups of foals, those given hyperimmune plasma (1/16) and those not given hyperimmune plasma (5/19)." (Higuchi *et al.*: page 645, second full paragraph). Additionally, while the administration of hyperimmune plasma to foals maintained their ELISA antibody titres against *Rhodococcus equi* antigens to the established infection level, "other factors such as fibronectin, complement and cytokines in the hyperimmune plasma might also play a role." (Higuchi *et al.*: page 647, first paragraph). Therefore, Higuchi *et al.* do not suggest to one of ordinary skill in the art to isolate antibodies from the plasma to use as the passive immunity vaccine as in the claimed method.

Neither Prescott *et al.* or Higuchi *et al.*, either taken alone or in combination, would suggest to a person of ordinary skill in the art a method which provides isolated

antibodies as a passive immunity vaccine against *Sarcocystis neurona* in horses. Neither reference would convince a person of ordinary skill in the art that hyperimmune plasma as a passive vaccine protects against organisms such as the bacteria *Rhodococcus equi.* Neither reference even suggests a method for producing a passive immunity vaccine against the apicomplexan parasite *Sarcocystis neurona.* Liang *et al.* and Marsh *et al.* either taken alone or in combination, would not show or suggest to a person of ordinary skill in the art a method which provides isolated antibodies against the 16 and 30 kDa antigen together as the passive immunity vaccine in horses. Liang *et al.* actually teaches away from a method for producing a passive immunity vaccine which provides isolated antibodies against the 16 and 30 kDa antigen together. Therefore, the cited references would not lead a person of ordinary skill in the art to the claimed method.

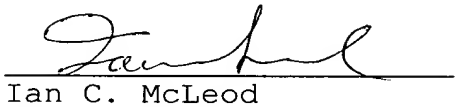
B. The Examiner rejected Claim 29 under 35 U.S.C. §112, second paragraph as being vague and indefinite.

In the Advisory Action, mailed July 07, 2005, the rejection under 35 U.S.C. §112, second paragraph was withdrawn by the Examiner.

C. Conclusion

As shown above, the claimed method is not obvious over the cited prior art references. Therefore, Claim 29 is patentable. Reversal of the Final Rejection is requested.

Respectfully,



Ian C. McLeod
Registration No. 20,931

McLEOD & MOYNE, P.C.
2190 Commons Parkway
Okemos, MI 48864

Telephone: (517) 347-4100
Facsimile: (517) 347-4103

CLAIMS APPENDIX

29. A method for producing an antibody for use as a passive immunity vaccine in horses against a *Sarcocystis neurona* antigen selected from the group consisting of a 16 (+/-4) kDa antigen and a 30 (+/-4) kDa antigen, as determined by SDS polyacrylamide gel electrophoresis, comprising:

(a) providing a *Sarcocystis neurona* antigen selected from the group consisting of the 16 (+/-4) kDa antigen and the 30 (+/-4) kDa antigen;

(b) admixing the antigen with an adjuvant to produce an admixture;

(c) immunizing a mammal with the admixture to produce antibodies against antigen;

(d) removing serum from the immunized mammal and isolating from the serum the antibody against the *Sarcocystis neurona* antigen selected from the group consisting of the 16 kDa +/-4 antigen and the 30 kDa +/-4 antigen; and

(e) providing the isolated antibodies to the 16 and 30 kDa antigen together as the passive immunity vaccine in horses.

EVIDENCE APPENDIX

(None.)

RELATED PROCEEDINGS APPENDIX

Attached are copies of the following:

1. Decision by the Board for Application No. 09/670,355.

2. Decision by the Board for Application No. 09/670,096 (Appeal No. 2005-2386).

3. Decision by the Board for Application No. 09/669,843 (Appeal No. 2004-1976).

Paper No. 13

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LINDA S. MANSFIELD, MARY G. ROSSANO, ALICE J. MURPHY and RUTH VRABLE

Appeal No. 2003-1919
Application No. 09/670,355

ON BRIEF

Before WILLIAM F. SMITH, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 10-12, 18-20, 44, 45 and 47-52. Claims 10 and 51 are representative of the subject matter on appeal, and read as follows:

> 10. A vaccine for protecting an equid from a Sarcocystis neurona infection comprising a DNA from Sarcocystis neurona that encodes at least a 16 ± 4 kDa antigen and/or 30 ± 4 kDa antigen of Sarcocystis neurona.

Co: 9.

51. A vaccine composition which comprises an effective immunizing amount of DNA derived from Sarcocystis neurona capable of inducing an antibody immune response, and a pharmacologically acceptable carrier.

Claims 10-12, 18-20, 44, 45 and 47-52 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, i.e., lack of adequate written description. In addition, claims 10-12, 18-20, 44-45 and 47-52 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, i.e., lack of enablement. Finally, claims 51 and 52 stand rejected under 35 U.S.C. § 112, second paragraph. After careful review of the record and consideration of the issues before us, we affirm the rejection of claims 10-12, 18-20, 44-45 and 47-52 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, and the rejection of claims 51 and 52 under 35 U.S.C. § 112, second paragraph, and decline to reach the merits of the rejection of claims 10-12, 18-20, 44-45 and 47-52 under 35 U.S.C. § 112, first paragraph, for lack enablement.

DISCUSSION

1. Rejection under 35 U.S.C. § 112, first paragraph, written description

Claims 10-12, 1-20, 44, 45 and 47-52 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, i.e., lack of adequate written description.

According to the rejection, "[r]eview of the present specification, the art of record, and a search of the sequence databases for polynucleotides and/or polypeptide sequences of 16(±4) kD antigen and the 30(±4) kD antigen indicate that these sequences have not been identified nor described." Examiner's Answer, page 4. The rejection further contends "the limitation 'at least' in the claims does not limit the invention to 16(±4) kD and/or 30(±4) kD antigen of S. neurona and broadly reads on any antigen that is not disclosed. The specification describes general methods of cloning cDNA sequences from expression libraries; however, the sequences obtained by this method for 16(±4) kD and/or 30(±4) kD antigen are not disclosed." Id. at 4-5. The rejection concludes that "the claimed invention as a whole is not adequately described and is not conventional in the art as of Appellants' effective filing date." Id. at 5 (emphasis in original).

With respect to the issue of conception in the context of an interference count, the Court of Appeals for the Federal Circuit, our reviewing court, has stated that "irrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance requires a definition of that substance other than by its functional utility." Fiers v. Revel, 984 F.2d 1164, 1169, 25 USPQ2d 1601, 1604 (Fed. Cir. 1993). The court specifically rejected Fiers' argument "that the existence of a workable method for preparing a DNA establishes conception of that material." Id.

In Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 2002), in determining whether or not a claim to a nucleotide sequence met the written description requirement, the court adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The court stated that:

> The written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.

Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613 (citations omitted).

In construing the above requirement, the court in In re Wallach, 378 F.3d 1330, 71 USPQ2d 1939 (Fed. Cir. 2004), recognized "that the written description requirement can in some cases be satisfied by functional description." Id., 378

F.3d at 1335. The court held, however, that

> such functional description can be sufficient only if there is also a structure-function relationship known to those of ordinary skill in the art. As we explained above, such a well-known relationship exists between a nucleic acid molecule's structure and its function in encoding a particular amino acid sequence: Given the amino acid sequence, one can determine the chemical structure of all nucleic acid molecules that can serve the function of encoding that sequence. Without that sequence, however, or with only a partial sequence, those structures cannot be determined and the written description requirement is consequently not met.

Id.

In the instant case, as noted by the rejection, neither the disclosure as filed, nor the prior art, discloses any sequence, either amino acid or nucleic, for either the 16(±4) kD and/or 30(±4) kD antigens. Consequently, the written description requirement is not met, and the rejection is affirmed.

Appellants argue with respect to the rejection of claims 10-12, 18-20, 44, 45 and 47-50 that they had "possession of Sarcocystis neurona which contains DNA encoding the 16 ±4 and 30 ±4 antigens. Thus, the applicants have possession of Sarcocystis neurona DNA encoding the 16 ±4 and 30 ±4 antigens." Appeal Brief, page 7. Appellants argue further that "[c]onstructing and screening an expression library for clones containing DNA encoding a particular protein is routine in the art," and thus "a person of ordinary skill in the art following the applicants' disclosure would have a high expectation of success of recovering clones from an expression library that express the 16 ±4 or 30 ±4

antigens using the antibodies against the 16 ±4 and 30 ±4 antigens prepared as taught in Example 1." Id. at 8.

Appellants' arguments are not convincing. First, the fact that appellants had possession of Sarcocystis neurona is not sufficient to provide possession of DNA that encodes the 16 ±4 and 30 ±4 antigens. As noted above, even a partial amino acid sequence of the 16 ±4 and 30 ±4 antigens, which would necessarily require possession of the source of the DNA, i.e., possession of Sarcocystis neurona, would not be sufficient to provide written description support for the claimed DNA encoding the 16 ±4 and 30 ±4 antigens. In addition, as also discussed above, the existence of a workable method to obtain the DNA sequence is also not sufficient to demonstrate written description support.

With respect to claims 51 and 52, appellants argue that appellants have possession of Sarcocystis neurona DNA, which "would be expected to encode a plurality of antigens, including the 16 ±4 and 30 ±4 antigens. Therefore, when the DNA is inoculated into a horse, the antigens encoded thereon are expressed in the horse." Appeal Brief, page 10. According to appellants, "[c]laims 51 and 52 do not depend on knowing the DNA sequences encoding the plurality of antigens. The claims merely require that the DNA encode one or more Sarcocystis neurona antigens. Thus, the DNA can be the entire Sarcocystis neurona genome(intact or fragmented) or particular DNA fragments therefrom." Id. at 11.

The above argument is also not found to be convincing. The disclosure as filed does not provide written description support for the use of the entire Sarcocystis neurona genome (intact or fragmented) or particular DNA fragments therefrom as a DNA vaccine. The written description is limited to a "DNA vaccine that contains or expresses at least one epitope of an antigen that has an amino acid sequence substantially similar to a unique 16 (±4kDa) antigen and/or 30 (±4) kDa antigen of Sarcocystis neurona." Specification, page 1 (Field of the Invention); see also pages 5, 17, 24 and 26. Thus, the rejection of claims 51 and 52 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, is affirmed for the reasons set forth supra with respect to the discussion of claims 10-12, 18-20, 44, 45 and 47-50.

2. Rejection under 35 U.S.C. § 112, second paragraph

Claims 51 and 52 stand rejected under 35 U.S.C. § 112, second paragraph, "as being vague and indefinite in the recitation of 'derived'. Is this DNA isolated from S. neurona?" Examiner's Answer, page 9.

This rejection is affirmed in view of appellants' statement that they will amend the term "derived" to "isolated." See Appeal Brief, page 20.

CONCLUSION

The rejection of claims 10-12, 1-20, 44, 45 and 47-52 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, and the rejection of claims 51 and 52 under 35 U.S.C. § 112, second paragraph are affirmed. Because we affirm the rejection under 35 U.S.C. § 112, first paragraph, on the

basis of lack of adequate written description, we decline to reach the merits of the rejection under 35 U.S.C. § 112, first paragraph, for lack enablement.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
Administrative Patent Judge)
)
)
)
) BOARD OF PATENT
)
Eric Grimes) APPEALS AND
Administrative Patent Judge)
)
) INTERFERENCES
)
Lora M. Green)
Administrative Patent Judge)

MCLEOD & MOYNE, P.C.
2190 COMMONS PARKWAY
OKEMOS, MI 48864

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

IAN C. McLEOD

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LINDA S. MANSFIELD, MARY G. ROSSANO, ALICE J. MURPHY and RUTH A. VRABLE

Appeal No. 2005-2386
Application No. 09/670,096

ON BRIEF

Before GRIMES, GREEN, and LEBOVITZ Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 2 and 21,[1] all of the pending claims, which are reproduced below:

[1] An amendment after final was filed concurrently with the Appeal Brief, dated August 20, 2004, and stamped August 23, 2004. Appellants state in the Appeal Brief that an Amendment was filed August 20, 2004, and in response, the examiner in the Examiner's Answer merely states that appellants' statement is correct, but does not explicitely state that the amendment was entered. But because the rejection of claim 2 under 35 U.S.C. § 112, second paragraph, for lack of antecedent basis was withdrawn, and the amendment after final remedied that issue, we infer that the amendment was entered. Thus, the claims as reproduced here are as amended by the August 23, 2004, amendment after final.

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Hudson
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1. A composition for treating an equid infected with Sarcocystis neurona comprising a mixture of isolated antibodies against a 16 ±4 kDa antigen of Sarcocystis neurona and isolated antibodies against a 30 ±4 kDa antigen of Sarcocystis neurona wherein the antibodies are from serum of an animal immunized with the antigen and wherein the mixture is in a pharmaceutically acceptable carrier.

2. The method of claim 21 wherein the antibodies are monoclonal antibodies.

21. A method for treating an equid infected with Sarcocystis neurona comprising:

(a) providing a mixture of antibodies against a 16 ±4 kDa antigen and a 30 ±4 kDa antigen, both of which are specific to Sarcocystis neurona, wherein the antibodies are selected from the group consisting of polyclonal antibodies from serum from an animal immunized with the antigen and monoclonal antibodies from a hybridoma, and wherein the antibodies are in a pharmaceutically acceptable carrier; and

(b) inoculating the equid with the antibodies in the carrier to treat the equid.

The claims stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way so as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention. After careful review of the record and consideration of the issue before us, we reverse.

DISCUSSION

Claims 1, 2 and 21 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first

paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) (emphasis in original). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." Id. at 224, 169 USPQ at 370. Here, the examiner has not provided "acceptable evidence or reasoning which is inconsistent" with the specification, and therefore has not met the initial burden of showing nonenablement.

In making the enablement rejection, the examiner engages in the analysis of the factors as set forth in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Examiner's Answer, page 5.

The examiner notes that given the high rate of exposure of horses to S. neurona and the low incidence of clinical equine protozoal myeloencephalitis (EPM), "indicate[s] that most horses develop effective immunity (no clinical symptoms of disease) that may prevent merozoite entry into the central nervous system." Id. at 6. The examiner goes on to state that the pathogenesis of the disease is not fully understood, and that clinical manifestations of the disease only occur in a small percentage of seropositive horses, citing Cutler[2] in noting

[2] Cutler et al. (Cutler), "Immunoconversion against Sarcocystis neurona in normal and dexamethasone-treated horses challenged with S. neurona sporocysts," Veterinary Parasitology, Vol. 95, pp. 197-210 (2001).

that "it is important and necessary to identify factors that govern progression from an apparent infection to clinically evident neurological disease, EPM . . . in horses." Id.

According to the examiner, "[t]he treatment of S. neurona infection in an equid with antibodies is highly complex and unpredictable because relative to the infection, the development of clinical spreading of the disease i.e., merozoite entry into the central nervous system crossing blood brain barrier is not known as most of the horses develop immunity without EPM." Examiner's Answer, page 6. As "the prior art does not teach administration of a mixture of isolated antibodies against a 16 kD antigen of S. neurona and isolated antibodies against a 30 kD antigen of S. neurona to an infected horse with EPM which would resolve the infection in CNS[,] . . . [t]hus there is a lack of understanding in the art with respect to the pathogenesis of S. neurona infection in horses that develop EPM." Id. at 7.

The examiner also relies on Liang 1998[3] to support the proposition that "not all antibodies generated during infection will neutralize the merozites." Examiner's Answer, page 7. The examiner asserts that from Liang 1998 it appears that extended exposure to antiserum appears to be necessary, and that in vitro data do not necessarily correlate to the results that will be obtained in vivo. See id. Moreover, according to the examiner, "it is unclear whether such

[3] Liang et al. (Liang 1998), "Evidence that Surface Proteins Sn14 and Sn16 of *Sarcocystis neurona* Merozoites Are Involved in Infection and Immunity," Infection and Immunity, Vol. 66, No. 5, pp. 1834-1838 (1998).

an immunotherapy can be used to treat all horses that are infected with S. neurona." Id. at 8. The examiner is also concerned that the specific antibodies used in the claimed immunotherapeutic methods are not characterized. See id.

We do not find that the examiner has provided evidence and/or reasoning that the claims are not enabled by the specification. As noted by appellants, "since many horses exposed to Sarcocystis neurona do not have clinical signs of EPM but have immunity to Sarcocystis neurona the serum antibodies are likely effective for protecting against the parasite." Appeal Brief, page 9. Given that, as further noted by appellants, "it would appear to be reasonable to believe that horses with EPM have an inadequate immune response to the parasite which is not sufficient to prevent entry of the parasite into the CNS and that boosting the immune response with antibodies against the 16 and 30 kDa antigens might provide a sufficient boost to an infected horse's immune response to inhibit entry of the parasite into the CSF." Id. at 16.

Moreover, Liang 1998 teaches that Sarcocystis neurona is sensitive to specific antibodies, and thus does not support the examiner's contention that the claims are not enabled. In regard to the examiner's statement that "it is unclear whether such an immunotherapy can be used to treat all horses that are infected with S. neurona," there is no requirement that the claimed method work with all horses that are infected with S. neurona.

In addition, Appellants submitted a declaration on April 1, 2003, Appendix B to the Appeal Brief, demonstrating that both the 16 and 30 kDa antigens

appeared to be more neutralizing than either antibody alone. See Appeal Brief, page 14. In response, the examiner argues that although "[t]he Declaration provides evidence that CSF from infected horses contains antibodies to 16kD and 30kD [antigens] and such antibodies neutralize the merozoites in vitro (neutralization assays) only," the declaration "does not provide any evidence that the claimed composition comprising said antibodies are useful for treating an equid infected with S. neurona." Examiner's Answer, page 13.

Thus, the examiner's principal concern appears to be that the specification provides no in vivo examples of treating a horse. See, e.g., Examiner's Answer, pages 6 and 8. The examiner notes that the specification "only discloses that multiple isolates of merozoites have been obtained by culturing sporozoites from opossum," id. at 8, and that "[t]he specification . . . provides no working examples demonstrating . . . enablement for the claimed composition or a method that is required in this under developed art. The specification only teaches culturing sporocysts and merozoites," id. at 9.

The presence or absence of a working example, however, is not determinative on the issue of enablement. It is just one factor that is to be weighed with the other factors. In the case at issue, the examiner has not met the burden of demonstrating that the specification does not enable the claims, and the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement, is reversed.

OTHER ISSUES

Appellants' and the examiner's attention is directed to related Appeal Number 2004-1976, U.S.S.N. 09/669,843. That appeal contained a claim to:

> A monoclonal mixture comprising an antibody that selectively binds to a 16 ± 4 kDa antigen of Sarcocystis neurona and a monoclonal antibody that selectively binds to a 30 ± 4 kDa antigen of Sarcocystis neurona wherein the antigens are separately isolated from Sarcocystis neurona merozoites by two-dimensional polyacrylamide gel electrophoresis and separately used to produce hybridomas which produce the monoclonal antibodies for the mixture.

In the 2004-1976 appeal, we affirmed a rejection under 35 U.S.C. § 103(a) over the combination of Liang 1998 or Liang 1997[4] and Harlow.[5]

Similarly, in the instant appeal, claim 1 is directed to:

A composition for treating an equid infected with Sarcocystis neurona comprising a mixture of isolated antibodies against a 16 ±4 kDa antigen of Sarcocystis neurona and isolated antibodies against a 30 ±4 kDa antigen of Sarcocystis neurona wherein the antibodies are from serum of an animal immunized with the antigen and wherein the mixture is in a pharmaceutically acceptable carrier.

The recitation of "for treating an equid infected with Sarcocystis neurona" is a statement of intended use, and not a patentable limitation. See In re

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[4] Liang et al. (Liang 1997), "Micropreparative High Resolution Purification of Proteins by a Combination of Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis, Isoelectric Focusing, and Membrane Blotting," Anal. Biochem., Vol. 250, pp. 61-65 (1997).

[5] Harlow et al. (Harlow, Antibodies, A laboratory Manual, Chapter 6, Col Spring Harbor Press (1988).

Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). Upon return of the appeal, the examiner may wish to consider the patentability of instant claim 1 in view of the references and the rejection as set forth in Appeal Number 2004-1976.

CONCLUSION

Because the examiner has not set forth a prima facie case of unpatentability, the rejection of claims 1, 2 and 21 under 35 U.S.C. § 112, first paragraph, for lack of enablement, is reversed. Upon receipt of the case, however, the examiner may wish to consider the patentability of claim 1 in view of the rejection under 35 U.S.C. § 103(a) as set forth in related Appeal 2004-1976.

REVERSED

Eric Grimes)
Administrative Patent Judge)
)
) BOARD OF PATENT
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Lora M. Green) APPEALS AND
Administrative Patent Judge)
) INTERFERENCES
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Richard M. Lebovitz)
Administrative Patent Judge)

MCLEOD & MOYNE, P.C.
2190 COMMONS PARKWAY
OKEMOS MI 48864

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LINDA S. MANSFIELD, MARY G. ROSSANO, ALICE J. MURPHY and RUTH A. VRABLE

Appeal No. 2004-1976
Application No. 09/669,843

ON BRIEF

Before WILLIAM F. SMITH, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 36, 51 and 52. The claims read as follows:

> 36. A monoclonal antibody that selectively binds to a 16 ± 4 kDa antigen of Sarcocystis neurona wherein the antigen is isolated from Sarcocystis neurona merozoites by two-dimensional polyacrylamide gel electrophoresis and used to produce a hybridoma which produces the monoclonal antibody.
>
> 51. A monoclonal antibody that selectively binds to a 30 ± 4 kDa antigen of Sarcocystis neurona wherein the antigen is isolated from Sarcocystis neurona merozoites by two-dimensional

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polyacrylamide gel electrophoresis and used to produce a hybridoma which produces the monoclonal antibody.

52. A monoclonal mixture comprising an antibody that selectively binds to a 16 ± 4 kDa antigen of Sarcocystis neurona and a monoclonal antibody that selectively binds to a 30 ± 4 kDa antigen of Sarcocystis neurona wherein the antigens are separately isolated from Sarcocystis neurona merozoites by two-dimensional polyacrylamide gel electrophoresis and separately used to produce hybridomas which produce the monoclonal antibodies for the mixture.

The examiner relies upon the following references:

Liang et al. (Liang 1997), "Micropreparative High Resolution Purification of Proteins by a Combination of Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis, Isoelectric Focusing, and Membrane Blotting," Anal. Biochem., Vol. 250, pp. 61-65 (1997).

Liang et al. (Liang 1998), "Evidence that Surface Proteins Sn14 and Sn16 of *Sarcocystis neurona* Merozoites Are Involved in Infection and Immunity," Infection and Immunity, Vol. 66, No. 5, pp. 1834-1838 (1998)

Harlow et al. (Harlow), Antibodies, A Laboratory Manual, Chapter 6, Cold Spring Harbor Press (1988).

Claims 36, 51 and 52 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Liang 1998 or Liang 1997 and Harlow. After careful review of the record and consideration of the issue before us, we affirm.

DISCUSSION

The claims stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Liang 1998 or Liang 1997 and Harlow.

Liang 1998 is cited for teaching the identification of S. neurona merozoite antigens from samples from horses with neurological signs typical of equine

myeloencephalitis (EPM) or confirmed EPM. See Examiner's Answer, page 3. The antigens so identified include a 30 KD antigen and a 16 KD antigen, which, according to the reference, appear to be cell surface antigens of merozoites. See id. The examiner states that "[a] combination of the results of western-blot analysis (figure 1) and trypsin digestion (figure 3 B) suggests that these are important surface proteins that could be used in specific diagnosis of S. neurona infection, as candidate antigens for vaccine development and specific antibodies to these antigens lyse merozoites via complement or inhibit their attachment and penetration to host cells." Id. Liang 1998 is also cited for teaching that monoclonal antibodies are often used to study parasitic proteins. See id. The examiner acknowledges that while "[a]ntibodies to 16KD antigen not only recognized the 16KD antigen but also lysed the merozoites in in vitro neutralization assays . . . antibodies to 30KD recognized the 30KD antigen but could not inhibit in vitro neutralization of merozoites, as 30KD antigen appears to cross-react with serum obtained from horses infected with other Sarcocystis species." Id. at 4. The examiner concludes "[t]hus the prior art teaches 30KD, 16KD, 14KD and 11KD proteins as merozoite surface antigens that are involved in S. neurona infection and EPM and could be used in the specific diagnosis of S. neurona." Id.

Liang 1997 is cited for teaching "purified 30 KD and 19 KD (i.e. 16 KD +/- 4) antigens from S. neurona merozoites by using infected horses serum." Id.

The rejection acknowledges that "Liang 1998 or Liang 1997 does not teach monoclonal antibody that selectively binds to 16KD antigen or a monoclonal antibody that selectively binds to a 30KD antigen or a monoclonal antibody mixture." Id.

Harlow is cited for teaching methods for "making monoclonal antibodies to any given antigen." Id.

The rejection concludes:

> It would have been prima facie obvious to one, having ordinary skill in the art at the time the invention was made to make monoclonal antibodies to merozoite surface antigens including 16KD and 30KD because Liang [ ] taught detection of S. Neurona infection using serum and sometimes infected horse serum cross reacts with antigens such as 30KD. Further, the art suggests monoclonal antibodies are often used to study parasite (page 1837, last paragraph) proteins and EPM disease occurs after merozoite passes through the vascular endothelium of blood-brain barrier into the central nervous system, and so humoral responses play essential role in blocking this migration and specific cytotoxic T cells are ineffective in attacking merozoite migration to the central nervous system in the blood stream (pag[e] [sic] 1837, left column, third paragraph). Therefore an artisan of ordinary skill would have been motivated to use readily available and purified surface antigens (Liang [ ] 1997) from merozoites including 16KD and 30 KD as disclosed by the prior art Liang [ ] 1998 or Liang [ ] 1997 with a reasonable expectation of success for raising monoclonal antibodies by using well established hybridoma technology as taught by [Harlow] because Liang [ ] 1998 suggests that humoral immunity to S. neurona infection is important (see page 1836 under discussion) especially in EPM disease and surface antigens including 30KD, 16KD, 14KD are immunoreactive with infected serum that are useful for the detection of the pathogenic S. neurona and Liang [ ] 1997 teach purification of target merozoite proteins 19 KD, 30 KD and 100KD. Moreover, it has become routine in the art to make monoclonal antibodies for characterizing and purifying proteins especially target proteins such as surface proteins of parasites or envelope proteins of bacteria.

Id. at 4-5.

We initially note that we find the Liang 1997 reference to be cumulative to the Liang 1998 reference, thus we focus our analysis on the Liang 1998 reference.

It is axiomatic that "the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. '[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.'" In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citation omitted). An adequate showing of motivation to combine requires "evidence that 'a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.'" Ecolochem, Inc. v. Southern Calif. Edison Co., 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1076 (Fed. Cir. 2000). We find that the rejection establishes a prima facie case of obviousness that has not been rebutted by appellants, and the rejection is affirmed.

Appellants argue that the combination does not provide any motivation to make the claimed monoclonal antibodies or the claimed mixture of antibodies. See Appeal Brief, page 6. Appellants acknowledge that "[g]enerating antibodies to a given antigen or epitope may have become routine in recent years," id. at 7,

but contend that "[t]here must also be a clear objective or motivation for one skilled in the art to combine the prior art." See id. Appellants assert that "the prior art references do not identify any need for making antibodies against the [16 and 30] kDa antigens or identify any problem that the antibodies could be used to solve." Id. at 14. Appellants contend that the rejection apparently relied on the "notion that making antibodies is routine" to provide the motivation to combine Liang 1998 with Harlow, which, according to appellants, is an impermissible hindsight rejection. See id. at 14.

Appellants argue with respect to claims 51 and 52 that the ordinary artisan would not have had motivation to make antigens against the 30 kDa antigen, because, while Liang 1998 suggests that the 16 kDa antigen appears to be an important antigen, Liang 1998 "suggests that the 30 kDa antigen is not important because it had no inhibitory activity and antibodies against the antigen were not recognized to be specific." Appeal Brief, page 15 (references omitted). Thus, appellants conclude, the ordinary artisan would not have been motivated to produce monoclonal antibodies against the 30 kDa antigen as in claim 51, or to produce a mixture containing that antibody as in claim 52.

Appellants' arguments are not convincing. As noted by the rejection, Liang 1998 specifically teaches that "monoclonal antibodies are often used to study parasitic proteins." See Liang 1998, page 1837, Col. 2. Moreover, Liang 1998 also teaches that *Sarcocystis neurona* is the etiologic agent of equine protozoal myeloencephilitis, see Liang 1998, page 1834, Abstract and Col. 1,

thus providing motivation to study and detect the parasite. Liang 1998 also teaches that antibodies specific for the 16 kDa antigen have protective activity against *S. neurona* and "support the use of the immunoblot test in diagnosis of [equine protozoal myeloencephilitis]," thus providing motivation to generate antibodies against the 16 kDa antigen.

With respect to the 30 kDa antigen, although Liang 1998 teaches that the antibodies are immunoreactive with sera from horses, infected with other *Sarcocystis*, it also teaches that monoclonal antibodies are often used to study parasitic proteins. Therefore, one of ordinary skill would have been motivated to produce antibodies to the 30 kDa antigen in order to study the antigen in *S. neurona* and other *Sarcocystis*. And one of ordinary skill would understand that a mixture of monoclonal antibodies to the 16 and 30 kDa antigens would allow one to determine if *Sarcocystis* other than *S. neurona* were present in horses with equine protozoal myeloencephilitis.

Appellants argue further that the combination of Liang 1998 and Harlow does not enable one skilled in the art to prepare antibodies against the 16 and 30 kDa antigens. See Appeal Brief. While, according to appellants, Liang 1998 demonstrates that the antigens are antigenic in horses, Harlow relates to the production of monoclonal antibodies in mice, and there is no teaching or suggestion in Liang 1998 that the antigens would produce antibodies, i.e., be antigenic, in mice. See id. at 11-12. Appellants distinguish Ex parte Erlich, 3 USPQ2d 1001 (Bd. Pat. App. & Int. 1986) by arguing that "because even though

Liang . . . (1998) show[s] that the 16 and 30 kDa antigens are antigenic, there is no prior art which shows that the method of [Harlow] could be adapted to produce monoclonal antibodies against the [16 and 30] kDa antigens." Id. at 13-14. Appellants conclude that the prior art does not provide a reasonable expectation of success that monoclonal antibodies could be generated against the 16 and 30 kDa antigens. See id. at 14.

Again, appellants' arguments are not found to be convincing. As acknowledged by appellants, methods for obtaining and screening for monoclonal antibodies were well known at the time of invention. See also In re Wands, 858 F.2d 731, 736, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Because the 16 and 30 kDa antigens from *S. neurona* were antigenic in horses, one of ordinary skill in the art would expect them to be antigenic in other mammals, such as mice. Moreover, appellants themselves refer to the 16 and 30 kDa proteins from *S. neurona* as antigens, and define an antigen as "a substance which stimulates production of antibody or sensitized cells during an immune response," Specification, page 12, thus one of ordinary skill would expect the 16 and 30 kDa antigens from *S. neurona* to be antigenic in mice. Finally, all that is required is a reasonable expectation of success, not absolute predictability of success. See In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

CONCLUSION

Because the examiner has established a prima facie case of obviousness that has not been rebutted by appellants, the rejection of claims 36, 51 and 52 under 35 U.S.C. § 103(a) is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

) BOARD OF PATENT
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MCLEOD & MOYNE, P.C.
2190 COMMONS PARKWAY
OKEMOS, MI 48864